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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,370	08/09/2000	Kuanghui Lu	ESCL-P02-060	5518

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,370	LU ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55,57,59-61,63-66,68,69 and 71-81* is/are pending in the application.

4a) Of the above claim(s) *1-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,57,59-61,63-66,68-69,71-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed October 20, 2003. Amendments were made to the claims.

Claims 1-55, 57, 59-61, 63-66, 68, 69 and 71-81 are pending in the instant application. Claims 1-54 are withdrawn as being drawn to a non-elected invention. Claims 55, 57, 59-61, 63-66, 68, 69 and 71-81 are under consideration in the instant application. Any rejection of record in the previous Office Action, mailed April 18, 2003, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55, 57, 59-61, 63-66, 68, 69 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for the reasons set forth in the previous Office Action**.

Claims 55, 57, 59-61, 63-66, 68, 69 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for the reasons set forth in the previous Office Action**.

Response to Arguments Concerning Claim Rejections - 35 USC § 112

Applicant's arguments filed October 20, 2003 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal as it relates to the rejection under Written Description:

1. Applicant points to several locations in the instant specification, stating that the cited passages illustrate a structure-function relationship for the broad genus of growth factors that can be used in the claimed invention. Specifically, Applicant asserts that pages 6 (lines 19-35), 7 (lines 1-12), 20 (lines 1-34), 25 (lines 3-35) and 26 (lines 1-29), as well as Examples 1, 2, 6 and 7 "includes not only the names of these known agents, but also a discussion of their structural and functional properties." Applicant concludes that these teachings combined with what was known in the prior art are sufficient to meet the requirements of 35 USC § 112 first paragraph, Written Description (see for example Applicant's Remarks on page 14, first paragraph).

2. Applicant contends the lists of exemplary agents, and the mere "utterance of the term fibroblast growth factor or dexamethasone immediately allows one of skill in the art to envision

the agents for use in the subject methods" (see for example Applicant's remarks on page 15, first paragraph).

Applicant's arguments are not convincing for the following reasons:

1 and 2. Applicant points to two specific places that are alleged to describe a structure-function relationship for the growth factors, page 6 and page 20. It is noted that in these locations, the specification simply lists a number of growth factors, such as EGF, HGF, FGF and TGFβ, although it is unclear that there is a specific description of a structure-function relationship between this compounds as it relates to the instant invention. As it regards a structure-function relationship for these compounds, one must be able to envision which growth factors can be used to prepare a substantially pure (i.e., at least 75% pure) population of non-adherent pancreatic or hepatic progenitor cells. Importantly, in Example 1, the specification clearly indicates that neither HGF nor TGFβ (two of the growth factors alleged to have a structure-function relatioship in the claimed method) had a significant effect on the non-adherent cell (NAC) population (see for example page 42, lines 3-4), while DCE (containing EGF) in contrast provided an enhanced proportion of NAC (see for example page 41, lines 32-34). Thus, it is clear from this example that not all of the compounds set forth in the instant specification (even at the specific locations Applicant refers to in their arguments) have the functional capacity to prepare a substantially pure population of pancreatic progenitor cells. Furthermore, there is no functional explanation as to why the DCE composition has such a profound effect on the production of substantially pure populations of pancreatic progenitor NAC, making it impossible for the skilled artisan to extrapolate from this single functional example as to what other structures will necessarily render a 75% pure population of pancreatic progenitor NAC. This point was distinctly made in the

previous Office Action (see page 4 of the Office Action), to which Applicant has not provided a direct argument. Instead, Applicant has only provided general arguments that any of the growth factors listed on page 6 or page 20 can be used in the claimed method, while their own specification contradicts this argument (see above). Since not all of the growth factors indicated by Applicant have a function to correspond with the given structures as it regards the instant invention, there can be no structure-function relationship between these growth factors as it regards the instant invention. Therefore, as set forth previously, the method does not provide a Written Description for which growth factors can or cannot be used to prepare a substantially pure population of pancreatic or hepatic progenitor cells.

While Applicant can utter the term "Fibroblast Growth Factor" (FGF) and the skilled artisan can envision its function in the differentiation of cell types, as well as other growth factors that will have a similar effect on differentiation (albeit into different cell types), the skilled artisan cannot envision the function of all of these growth factors in relation to the preparation of pancreatic progenitor NAC. It is clear from Applicant's own specification that not all of the growth factors that are declared as having a structure-function relationship (at least in terms of cell differentiation) have a structure-function relationship with regard to the preparation of pancreatic progenitor NAC. As such, the skilled artisan cannot envision which of the growth factors (besides EGF as contained in the DCE composition) can necessarily be used to produce a substantially pure population of pancreatic progenitor cells of at least 75% purity. Thus, Applicant has not met the structure-function relationship standard of Written Description with regard to the instantly claimed invention, and the rejection is properly maintained.

Applicant's arguments filed October 20, 2003 have been fully considered but they are not persuasive. With respect to the Enablement rejection, Applicant provides the following grounds for traversal:

1. Applicant asserts that the Office has failed to make of record any references to support the non-enablement of the claimed invention, and therefore has failed to make a *prima facie* case of enablement (see for example Applicant's Remarks on page 16, last full paragraph).

2. Applicant alleges the Office is imposing upon Applicant an unduly high standard of enablement, suggesting that the Examiner *believes* Applicant is entitled only to claims for which working examples are provided.

3. Applicant raises the issue that there is no legal requirement that the claimed invention be supported with working examples. Applicant further provides the generalized statement that the level of skill in the art is very high, and the specification provides the skilled artisan with sufficient guidance such that undue experimentation is not required to practice the claimed invention.

Applicant's arguments are not convincing for the following reasons:

1. Applicant suggests that the Office has not provided a reference to support a *prima facie* case that the claims are not enabled. The Office disagrees with this statement, arguing that Applicant's own specification serves as a reference that provides a significant degree of unpredictability regarding which growth factor compositions can be used to necessarily produce a 75% pure population of pancreatic progenitor NPC. Indeed, the Office specifically indicates in the rejection that the instant specification provides the information that not all of the growth factor preparations were sufficient to enhance the population of NAC to a significant level (see

for example page 8 of the previous Office Action). Given this teaching that many of the growth factors tested did not accomplish the claimed method, while only one composition (DCE) clearly worked, the skilled artisan would not be apprised of how to perform the claimed method across the broad spectrum of growth factors that are encompassed by the claim. Indeed, it would be highly unpredictable (the standard for enablement) which other growth factor preparations would have a similar effect as the seemingly unique DCE composition with regard to the claimed method. As this entire line of reasoning was established in the previous Office Action, the Office maintains that it has established a *prima facie* case of a lack of enablement. It is noted that Applicant has not provided an argument pointing out the flaws in the factual representation of the teachings set forth in the Wands analysis of the previous Office Action.

2 and 3. It is not clear how the instant rejection is placing an unduly high standard of enablement upon the instant claims, nor does the Office feel they are requiring Working Examples of all enabled embodiments. The Office has simply considered all of the Wands factors as it relates to the instant claims, and set forth an enablement rejection. All of the Wands factors are represented in the rejection as originally presented, and Applicant has not pointed to any specific flaws in the reasoning of the rejection to substantiate their claim that the standards are unduly high. As stated in the rejection and addressed above in response to Applicant's arguments, Applicant's own specification clearly indicates that a number of growth factors do not have any substantial effect on the preparation of an at least 75% pure population of pancreatic progenitor cells. This teaching alone would cause the skilled artisan to legitimately question which growth factor preparations, aside from the DCE preparation, would be suitable to use the claimed method. This fact has nothing to do with what the Examiner *believes*, only what

the instant specification *teaches*. Additionally, it is not the single fact that the specification only teaches one functional composition that can be used in the method as claimed, but a combination of that fact along with the explicit teaching that many of the other growth factor compositions had no effect (again see for example page 41 (line 26) to page 42 (line 4)). As stated above, this raises a serious issue of unpredictability as to which compositions will have the *required effect* of producing a 75% pure (or better) population of pancreatic progenitor NAC. It is this unpredictability, and not the absence of working examples, that truly represents the nature of the enablement rejection. Importantly, although the previous Office Action raises the question of why only one composition worked while many others did not, Applicant does not provide a reasonable argument to address that issue.

In conclusion, it is noted that Applicant specifically avoids the issue set forth in the enablement rejection concerning the inability of several growth factor compositions to have a significant effect on the production of an at least 75% pure population of progenitor NAC. Instead, Applicant provides very generalized arguments suggesting that the Office has not set forth a *prima facie* case of lack of enablement, and that Applicant is being held to an unduly high standard of enablement that requires all of the claimed embodiments to be presented in working examples. These general arguments do not point out legitimate and specific flaws in the Wands analysis provided in the previous Office Action. In response to the generalized arguments, the Office has reiterated its position regarding the unpredictability of which growth factor compositions can be used in the claimed invention, considering not only the fact that only a single compound seems to have given the required effect, but also that Applicant's own specification clearly indicates that many of the growth factors did not significantly enhance the

production of progenitor NAC such that a substantially pure population of 75% or greater could be obtained by the culturing methods alone. As a result, Applicant's arguments are not convincing, and the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 55, 63-65, 69, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-5, 8, 15, 25 and 26 of U.S. Patent No. 6,326,201. **This rejection is maintained for the reasons set forth in the previous Office Action**.

Since Applicant provides no arguments concerning the correctness of the rejection, no response can be made by the Office, and the rejection is maintained until the filing of a terminal disclaimer obviates the rejection.

Allowable Subject Matter

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER